REMARKS

Claims 1-30 are pending in the present application. By virtue of this response, claims 1-20, 24 and 28-30 have been canceled, claims 21-23, 25 and 26 have been amended and new claims 31-54 have been added. Accordingly, claims 21-23, 25-27, and 31-54 are currently under consideration.

Amendments and cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim Amendments

The amendments of claims 21-23, 25 and 26, as well as new claims 31-54, are fully supported by the original application. References to paragraph numbers herein are taken from the published U.S. application.

Claims 21-23, 25 and 26, either directly or indirectly, have been amended to recite an antisense oligonucleotide comprising a sequence substantially complementary to SEQ ID NO: 5, wherein the oligonucleotide is from about 8 to about 50 nucleotides in length. Support for the amendment "substantially complementary to SEQ ID NO: 5" can be found, for example, in paragraphs [0014], [0050] and [0099]. Support for the amendment "wherein the oligonucleotide is from about 8 to about 50 nucleotides in length" can be found, for example, in paragraphs [0062] and [0137].

New claims 31-54 find support throughout the application as filed. For example, support for new claims 31, 39, 44 and 49 can be found in paragraphs [0062], [0067], [0129] and [0137]. Sequences that are "substantially complementary" to a second sequence are understood to include, but not be limited to, sequences that are 100% complementary to the second sequence,

as evidenced by paragraphs [0067] and [0129]. New claims 32, 33, 40, 45 and 50 find support, for example, in paragraphs [0017], [0101] and [0132]. New claims 34, 36, 41, 46 and 51 find support, for example, in paragraphs [0062] and [0137]. New claims 35, 37, 42, 47 and 52 find support, for example, in paragraphs [0017], [0101], [0124], [0130] and [0132]. New claims 38, 43 and 48 find support, for example, in paragraphs [0023], [0024], [0025], [0106] and [0140]. New claims 53 and 54 find support, for example, in paragraphs [0027] and [0142].

Claim Rejections under 35 U.S.C. § 112

Claims 22 and 28 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, claims 22 and 28 both depend from withdrawn (now canceled) claim 1. Claim 22 has been amended to depend from claim 21, and claim 28 has been canceled. Accordingly, Applicants respectfully request that the rejections of claims 22 and 28 under U.S.C. § 112, second paragraph, be withdrawn.

Claims 23 and 26 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Claims 23 and 26 are rejected because the specification allegedly does not provide any disclosure for the use of the phrase "compound or agent" that inhibits the expression of mammalian KSR. Without acquiescing to the Office's assertions and in the interest of expediting prosecution, the phrase "compound or agent" has been removed and claims 23 and 26 have been amended to recite the phrase "an antisense oligonucleotide." Accordingly, Applicants respectfully request that the rejection of claims 23 and 26 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claims 23-25 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Claims 23-25 are rejected because the specification allegedly does not provide sufficient guidance such that one in the art would know how to prevent a hyperproliferative disease from manifesting. Without acquiescing to the Office's

assertions and in the interest of expediting prosecution, the phrase "or preventing" has been removed from claims 23 and 25. Claim 24 has been canceled. Accordingly, Applicants respectfully request that the rejection of claims 23-25 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claim Rejections under 35 U.S.C. § 102

Rejection of claims 21 and 22 over Yan et al.

Claims 21 and 22 are rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Yan et al. (Cancer Research, 2001). Applicants respectfully traverse this rejection.

Without acquiescing to the Office's assertions and in the interest of expediting prosecution, claims 21 and 22 have been amended. Claims 21 and 22, as amended, recite a method of inhibiting the expression of mammalian KSR comprising contacting cells which express KSR with an antisense oligonucleotide comprising a sequence substantially complementary to SEQ ID NO: 5, wherein the oligonucleotide is from about 8 to about 50 nucleotides in length. Applicants respectfully submit that Yan et al. does not anticipate these claims.

To anticipate a claim, a prior art reference must teach or suggest each and every limitation of the claim. Yan et al. does not teach or suggest antisense oligonucleotides. Neither does Yan et al. teach or suggest a method of inhibiting the expression of KSR using antisense oligonucleotides targeted to specific sequences of KSR mammalian RNA. In addition, Yan et al. does not teach or suggest methods of treating hyperproliferative conditions, such as cancer, wherein the methods comprise administering an antisense oligonucleotide to a mammal.

Accordingly, Yan et al. does not teach or suggest each and every element of claims 21 and 22, as amended. Applicants respectfully request that the rejection of claims 21 and 22 under 35 USC § 102(a) be withdrawn.

Rejection of claims 21, 22, 26 and 28 over Monia et al.

Claims 21, 22, 26 and 28 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Monia et al. (U.S. 2003/0109466). Applicants respectfully traverse this rejection.

As discussed above, claim 28 has been canceled. Claim 21 and 22 have been amended without prejudice to recite a method of inhibiting the expression of mammalian KSR comprising contacting cells which express KSR with an antisense oligonucleotide comprising a sequence substantially complementary to SEQ ID NO: 5, wherein the oligonucleotide is from about 8 to about 50 nucleotides in length. Similarly, claim 26, has been amended to recite a method of treating or inhibiting the progression of cancer in a mammal comprising administering to a mammal an antisense oligonucleotide comprising a sequence substantially complementary to SEQ ID NO: 5, wherein the oligonucleotide is from about 8 to about 50 nucleotides in length. Monia et al. does not anticipate any of these claims.

Specifically, Monia et al. neither teaches nor suggests an oligonucleotide substantially complementary to a sequence of SEQ ID NO: 5, wherein the oligonucleotide is from about 8 to about 50 nucleotides in length. In fact, Monia et al. does not disclose any sequences comprising SEQ ID NO: 5 or any sequences substantially complementary to SEQ ID NO: 5, because the KSR sequence provided and referenced in Monia et al. is a partial or incorrect sequence and does not have SEQ ID NO: 5 or its surrounding sequence.

Accordingly, Monia et al. does not teach or suggest each and every element of claims 21, 22, and 26, as amended. Applicants respectfully request that the rejection of claims 21, 22, 26 and 28 under 35 USC § 102(e) be withdrawn

Claim Rejections under 35 U.S.C. § 103

Rejection of claims 21-28 over Monia et al.

Claims 21-24 and 26-28 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Monia et al. (U.S. 2003/0109466). Applicants respectfully traverse this rejection.

As a preliminary matter, Applicants respectfully submit that claims 24 and 28 are canceled. Claims 21-23 and 26 have been amended without prejudice in an effort to expedite prosecution. Claim 27 depends from rejected claim 26. Claims 21 and 22 as amended recite a method of inhibiting the expression of mammalian KSR comprising contacting cells which express KSR with an antisense oligonucleotide comprising a sequence substantially complementary to SEQ ID NO: 5, wherein the oligonucleotide is from about 8 to about 50 nucleotides in length. Claim 23 as amended recites a method of treating a hyperproliferative condition associated with the expression of gf-Ras or heightened expression of Ras in a mammal comprising administering to the mammal an antisense oligonucleotide comprising a sequence substantially complementary to SEQ ID NO: 5, wherein the oligonucleotide is from about 8 to about 50 nucleotides in length. Claim 26 as amended recites a method of treating or inhibiting the progression of cancer in a mammal comprising administering to the mammal an antisense oligonucleotide comprising a sequence substantially complementary to SEQ ID NO: 5, wherein the oligonucleotide is from about 8 to about 50 nucleotides in length. Monia et al. does not render any of the claims obvious.

To establish a *prima facie* case of obviousness, the prior art reference must teach or suggest all the claim limitations. As discussed above with respect to the rejection of claims 21, 22, 26 and 28 under § 102(e) over Monia et al., Monia et al. does not teach or suggest an antisense oligonucleotide comprising a sequence substantially complementary to SEQ ID NO: 5. In fact, Monia et al. does not disclose any sequences comprising SEQ ID NO: 5 or any sequences

substantially complementary to SEQ ID NO: 5. Similarly with regard to claims 23 and 27, Monia et al. neither teaches nor suggests an antisense oligonucleotide comprising a sequence substantially complementary to SEQ ID NO: 5.

Accordingly, Monia et al. does not teach or suggest each and every element of claims 21-24 and 26-28, as amended. Applicants respectfully request that the rejection of claims 21-24 and 26-28 under 35 USC § 103(a) be withdrawn.

Rejection of claim 25 over Monia et al. in view of Noonberg.

Claim 25 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Monia et al. (U.S. 2003/0109466) in view of Noonberg et al. (US 5,624,803). Applicants respectfully traverse this rejection.

Claim 25 has been amended without prejudice to recite a method of treating a hyperproliferative condition associated with the expression of gf-Ras or heightened expression of Ras in a mammal comprising expressing in the animal an antisense oligonucleotide comprising a sequence substantially complementary to SEQ ID NO: 5, wherein the oligonucleotide is from about 8 to about 50 nucleotides in length. Monia et al. and Noonberg et al., alone or in combination, do not render claim 25 obvious.

As discussed above, Monia et al. fails to teach an antisense oligonucleotide comprising a sequence substantially complementary to SEQ ID NO: 5, wherein the oligonucleotide is from about 8 to about 50 nucleotides in length.

Noonberg et al. does not cure the deficiency discussed above. Specifically, Noonberg et al. is cited as teaching the use of *in vivo* oligonucleotide generators for the effective expression of antisense in methods of treating disease in animals. Noonberg et al. does not teach or suggest an antisense oligonucleotide comprising a sequence substantially complementary to SEQ ID NO: 5, wherein the oligonucleotide is from about 8 to about 50 nucleotides in length.

Accordingly, Monia et al. in view of Noonberg et al. does not teach or suggest each and every element of claim 25 as amended. Applicants respectfully request that the rejection of claim 25 under 35 USC § 103(a) be withdrawn.

FEES

No fees are believed to be necessitated by the foregoing Response. However, should this be erroneous, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or credit any overages.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant application. The claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

Respectfully submitted,

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